FDAMA Section 113: The Clinical Trials Databank—What Should a Pharmacist Know?

Pharmacotherapy Frontiers
Continuing Education Seminar

April 22, 2006

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FDA

Goals

- Review the history and current status of Clinical Trials Registries and Clinical Trials Results Databases
- Focus on legislative, regulatory, and other initiatives impacting the development of the National Library of Medicine's ClinicalTrials.gov
- Discuss how data are received by ClinicalTrials.gov
- Demonstrate how to use ClinicalTrials.gov

Registry vs. *Results Database*

- A *clinical trials registry* provides information about ongoing clinical trials that are open and recruiting patients (e.g ClinicalTrials.gov).
- A *clinical trials results database* provides information about the results of clinical studies (e.g www.clinicalstudyresults.org)

ACTIS

The National Institute on Aging

Alzheimer's Disease Clinical Trials Database

NATIONAL LIBRARY OF MEDICINE

Office of Rare Diseases

National Institutes of Health

NATIONAL CANCER INSTITUTE

Publicly accessible clinical trials information in government sponsored databases is not a new concept.

CDC

www.actis.org

cancernet.nci.nih.gov

Rarediseases.info.nih.gov/ord

www.alzheimers.org/trials/index.html

FDA

Clinical Trial Registries and Results Databases History

The 1980's

- PDQ
  Cancer Trials
- ACTIS
  HIV/AIDS Trials

1997 Food and Drug Modernization Act (FDAMA Section 113)

- Directed DHHS Secretary to:

  establish, maintain, operate data bank on clinical trials for drugs to treat serious or life-threatening diseases and conditions.
- Modeled after 1988 HOPE legislation
- Purpose: primarily for patients

www.fda.gov/opacom/7modact.html

1997 Food and Drug Modernization Act (FDAMA Section 113)

Clinical trial listing MUST:

- Describe the trial's purpose
- Outline patient eligibility criteria
- List trial locations
- Include contact information for enrollment
- Be written in easily understood language

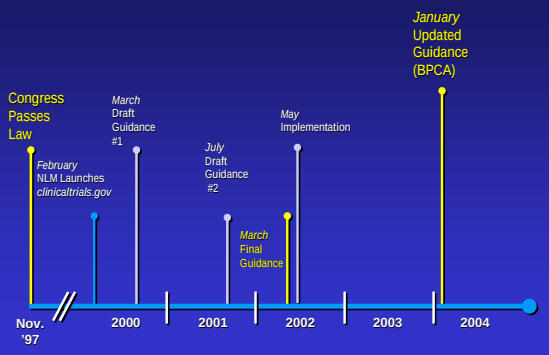
Listing trial results is VOLUNTARY

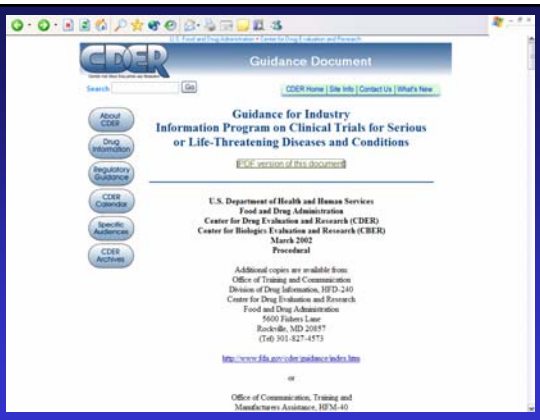
1997 Food and Drug Modernization Act FDAMA Section 113

- NIH - National Library of Medicine (NLM) with FDA and others.
- 1st version available to public February 29, 2000.
- 2000-2002, data bank included mainly NIH trials.
- Today, over 27,000 trials listed, from the public and private sectors.

ClinicalTrials.gov

Implementation Timeline





http://www.fda.gov/cder/guidance/4856fnl.htm

Clinical Trial Registries and Results Databases Recent History

Date	Event
June 2004	New York state Attorney General Eliot L. Spitzer alleged in a civil lawsuit that Glaxo systematically withheld negative information about Paxil.
September 2004	The ICMJE member journals will require, as a condition of consideration for publication, registration in a public trials registry. Trials must register at or before the onset of patient enrollment. This policy applies to any clinical trial starting enrollment after July 1, 2005.
October 2004	Kennedy/Dodd Bill S 2933 Draft and Markey/Waxman F.A.C.T. Bill HR 5252 Draft
January 2005	Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and related information. http://www.phrma.org/mediaroom/press/releases/06.01.2005.1112.cfm and 5.1114.cfm

Clinical Trial Registries and Results Databases
APhA House of Delegates, New Business (2005)

APhA supports the establishment of a single, independent, publicly accessible clinical trials database

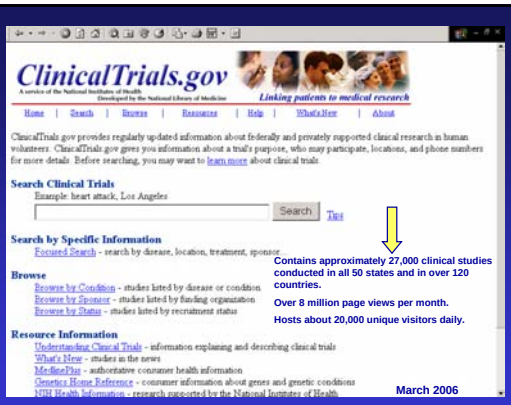
- includes all studies
- states the size, demographics, limitations and citations, if published, of each study listed
- explains the purpose of the study, methods and outcomes in lay-terms to assist in public understanding
- includes warnings to the public on use of data for clinical decision making
- includes full disclosure of sponsors/supporting organizations or companies

http://www.aphanet.org/AM/Template.cfm?Section=Search&section=APRS&template=/CM/ContentDisplay.cfm&ContentFileID=406

Clinical Trial Registries

Types of web sites

- Federal
- Commercial Third-Party
- Location-Specific
- Sponsor-Specific
- Patient Advocacy
- Other



ClinicalTrials.gov

Commercial Third-Party Sites

- Generally operated by private companies.
- Some trial listings copied from Federal sites and edited.
- Some obtain trial information directly from sponsors and clinical investigators.
- Generally funded through fees for listing, referral, enrollment, or advertising.
- Examples: Emerging Med, Veritas Medicine, Acurian, CenterWatch

www.centerwatch.com/

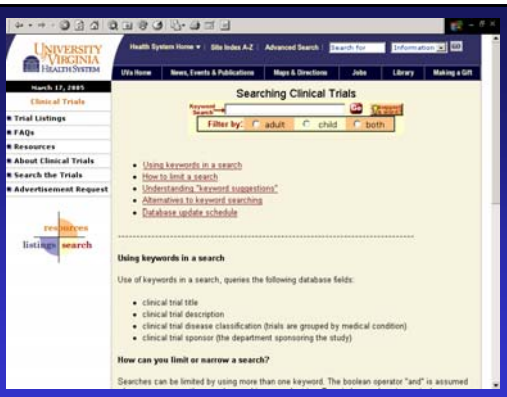
Patient Advocacy Sites

- Work on behalf of people diagnosed with a disease.
- May provide education, support, financial assistance, and advocacy to help patients and families.
- Educate and empower people to find information and access to treatment.
- May list trials from multiple sources, e.g. government, pharmaceutical companies, hospitals.
- Some trial listings are copied from Federal sites and edited.

www.lymphomation.org/clinical-trials-gov.htm

Location-Specific Sites

- Managed by a specific healthcare facility or its contractor.
- Includes mainly clinical trials being conducted at their location.
- Obtain trial information directly from clinical investigators at those locations.



www.healthsystem.virginia.edu/clinical_trials/search/searchinfo.cfm

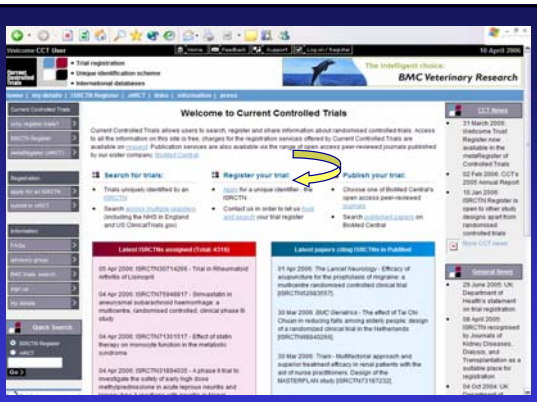
Sponsor-Specific Sites

- Managed by commercial sponsors of clinical trials or their contractors.
- Trials listed on these sites tend to be only those trials supported by the sponsor.

www.novartisclinicaltrials.com/etrials/home.do

Examples of Other Web Sites

- Current Controlled Trials Ltd
  - A *meta*Register allows searching across multiple registers.
- Stroke Trials Directory
  - Joint effort funded in part by grants from the National Institute of Neurological Disorders and Stroke.



http://controlled-trials.com/

www.strokecenter.org/trials/

What kind of information do these sites disclose?

- General Descriptive Trial Information
- Prescreening
- Disease Information
- Trial Folders
- E-Mail Updates
- Message Center
- Results
- Links

Clinical Trial "Results Databases"

- FDA sponsored
- PhRMA sponsored
- Company sponsored
- ClinicalTrials.gov

FDA "Results Databases"

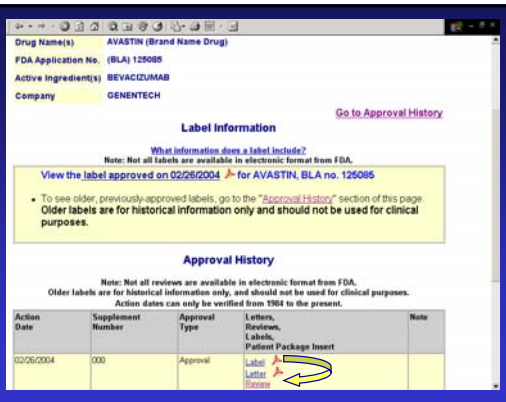
- Drugs
- Biologics
- Devices

FDA "Results Databases"

- Drugs@FDA
  - Includes most drug products approved since 1939
  - Includes majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

  www.accessdata.fda.gov/scripts/cder/drugsatfda/
- Best Pharmaceuticals for Children Act (BPCA)
  - Requires FDA to make available to the public a summary of the medical/clinical pharmacology reviews of the pediatric studies for the supplement.

  www.fda.gov/cder/pediatric/Summaryreview.htm



Drugs@FDA

Approved Medical Devices

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/MDA/mda-list.cfm?list=1

Approved Biological Products

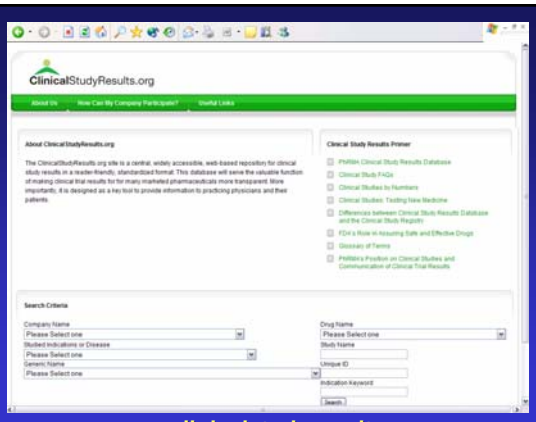
http://www.fda.gov/cber/efoi/approve.htm

PhRMA "Results Database"

September 07, 2004

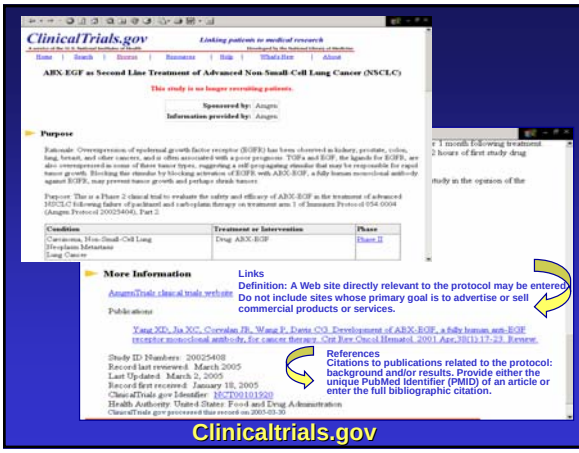
- **A central, easily accessible database to better communicate the results of clinical studies of marketed drugs at www.clinicalstudyresults.org.**
- **Will contain results of controlled clinical trials (mainly Phase III and IV studies), both positive and negative,completed since October 2002 for PhRMA-member company drugs approved in the US.**
- **Will include both published articles and unpublished study summaries.**

www.phrma.org/mediaroom/press/releases/07.09.2004.1063.cfm

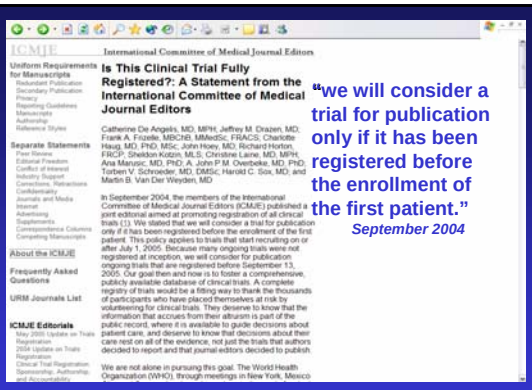


www.clinicalstudyresults.org

www.lillytrials.com/



Clinicaltrials.gov



ICMJE International Committee of Medical Journal Editors

Is This Clinical Trial Fully Registered?: A Statement from the International Committee of Medical Journal Editors

Catherine De Angelis, MD, MPH; Jeffrey M. Drazen, MD; Frank A. Frizelle, MBChB, MMedSc, FRACS; Charlotte Haug, MD, PhD, MSc; John Hoey, MD; Richard Horton, FRCP; Sheldon Kotzin, MLS; Christine Laine, MD, MPH; Ana Marusic, MD, PhD; A. John P.M. Overbeke, MD, PhD; Torben V. Schroeder, MD, DMSc; Harold C. Sox, MD; and Martin B. Van Der Weyden, MD

In September 2004, the members of the International Committee of Medical Journal Editors (ICMJE) published a joint editorial aimed at promoting registration of all clinical trials (1). We stated that we will consider a trial for publication only if it has been registered before the enrollment of the first patient. This policy applies to trials that start recruiting on or after July 1, 2005. Because many ongoing trials were not registered at inception, we will consider for publication ongoing trials that are registered before September 13, 2005. Our goal then and now is to foster a comprehensive, publicly available database of clinical trials. A complete registry of trials would be a fitting way to thank the thousands of participants who have placed themselves at risk by volunteering for clinical trials. They deserve to know that the information that accrues from their altruism is part of the public record, where it is available to guide decisions about patient care, and deserve to know that decisions about their care rest on all of the evidence, not just the trials that authors decided to report and that journal editors decided to publish.

We are not alone in pursuing this goal. The World Health Organization (WHO), through meetings in New York, Mexico

"we will consider a trial for publication only if it has been registered before the enrollment of the first patient."

September 2004

http://www.icmje.org/clin_trialup.htm

Weekly Trends (May – October 2005)

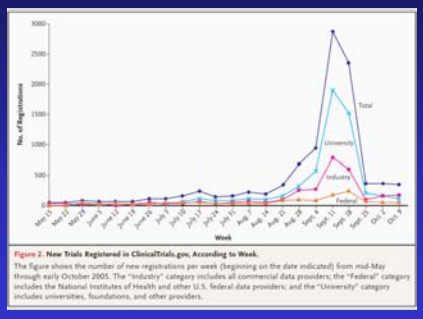


Figure 2. New Trials Registered in ClinicalTrials.gov, According to Week.

The figure shows the number of new registrations per week (beginning on the date indicated) from mid-May through early October 2005. The "Industry" category includes all commercial data providers; the "Federal" category includes the National Institutes of Health and other U.S. federal data providers; and the "University" category includes universities, foundations, and other providers.

(Source: Zarin et al. N Engl J Med. 2005;353:2779-87)

How is the information submitted?

Through a web-based Protocol Registration System (PRS) developed by NLM

prsinfo.clinicaltrials.gov/

Who submits the information?

- **A sponsor**
  - **multiple individuals as data providers**
  - **controls access by designating users and administrators**
- **Intermediaries acting on behalf of a sponsor , e.g. Centerwatch**

ClinicalTrials.gov Registration Requirements

ClinicalTrials.gov Data Element	Registration Requirements
Descriptive Information	
Brief Title (lay language)	Required
Official Title	WHO
Brief Summary (lay language)	Required
Detailed Description	
Study Phase	Required
Study Type (Interventional/Observational)	Required
Study Design*	Required
Primary Outcome Measure(s)	WHO
Secondary Outcome Measure(s)	WHO
Condition(s)	Required
Intervention: Type/Name	Required
MEDLINE PMID: Citation/Results Reference	
Link: URL/Description	
Recruitment Information	
Overall Recruitment Status	Required
Start Date	WHO
Completion Date	
Other Dates	
Eligibility Criteria	Required
Gender	Required
Age: Minimum/Maximum	Required
Accepts Healthy Volunteers?	
Target Number of Subjects	WHO

ClinicalTrials.gov Data Element	Registration Requirements
Location and Contact Information	
Facility Location	Required
Facility Recruitment Status	Required
Contact Information (Central or per Facility)	Required
Facility Investigators	
Overall Study Official(s)*	WHO
Administrative Data	
Unique Identifier (NCT #) - assigned by system	Automatic
Organization's Protocol ID Number	Required
Secondary Protocol ID Number(s)	WHO
FDA IND/IDE Protocol? (yes/no) *	Required
Human Subjects Review Approval? (yes/no) *	Required
Study Sponsor	Required
Collaborators	WHO
Record Verification Date	Required
First Received Date - assigned by system	Automatic

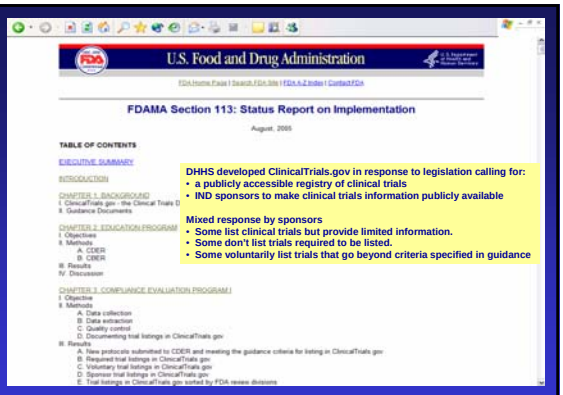
Boldfaced Print: Items required by ClinicalTrials.gov (incorporates FDAMA 113)

WHO: Items additionally required for ICMJE (WHO minimal registration data set)

* Additional information required in some instances

Italicized print: Items not displayed at the public site

prsinfo.clinicaltrials.gov/



http://www.fda.gov/oashi/clinicaltrials/section113/113report/default.htm

Questions to Consider

- Who is the information in a database/registry for?
- What information should a database/registry include?
- How is information standardized?
- What data are relevant to the general public?
- Who reviews the information before it is listed?

More Questions to Consider

- Should there be one registry or many linked together?
- Is reporting information voluntary or mandatory?
- Who pays for the database/registry and the upkeep?
- What is the physician's role?
- What is the impact of patient "study shopping?"

More Questions to Consider

- What are the concerns about intellectual property?
- How do intellectual property concerns relate to the public's right to know about research involving human subjects?
- Will IRBs be (more) overburdened?
- Will product development / approval decisions become politicized?
- And many more.

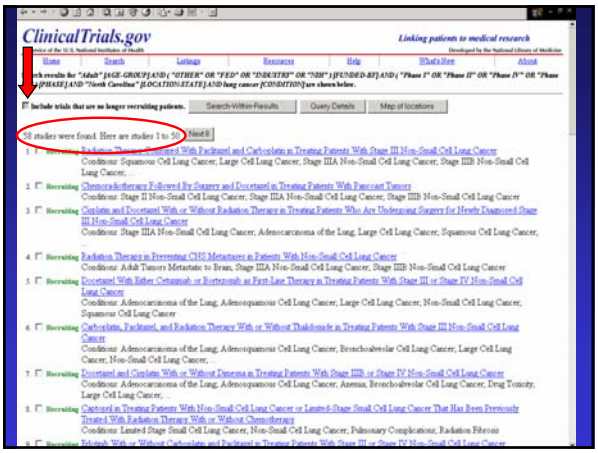
Case Study

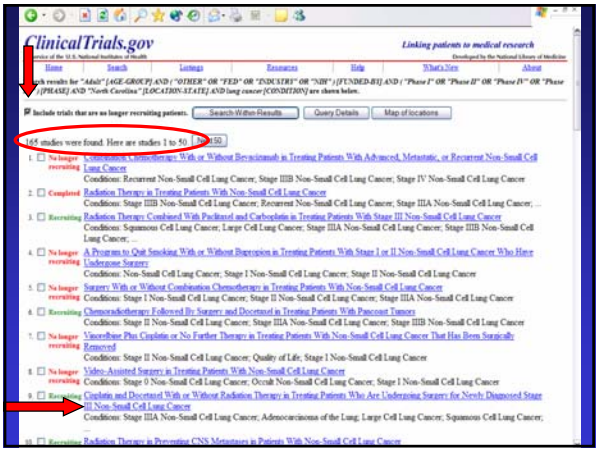
- Peter, a patient at your pharmacy
- 48 year old engineer
- Has non-small cell lung cancer and wants to learn about clinical trials
- Has a computer at home and regularly monitors new medical developments
- Works in partnership with his doctor
- Does not wish to travel outside of North Carolina

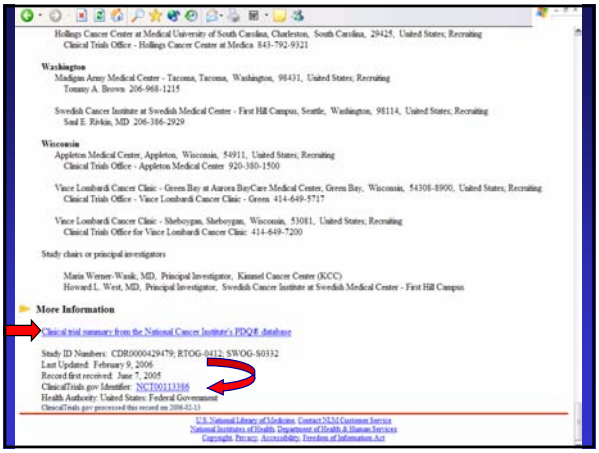
On the Focused Search page, enter words or phrases in the appropriate search box(es) and click on any of the check boxes to specify your search criteria.

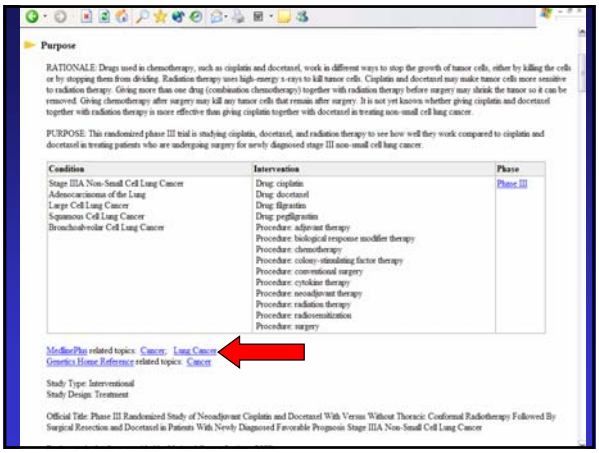
Using different search boxes and/or check boxes "focuses" your search and increases the precision of your results. Note that it is not necessary to fill in all the boxes, only those that are needed for your search.

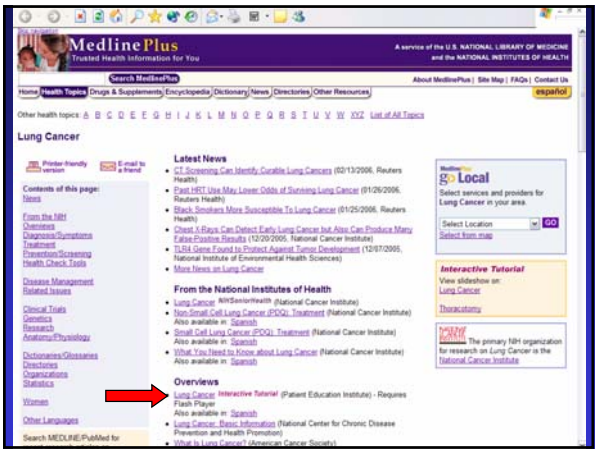
Disease or Condition
Specify health problems or conditions being studied.
Examples:
Lung cancer
Lupus
heart attack
leukemia



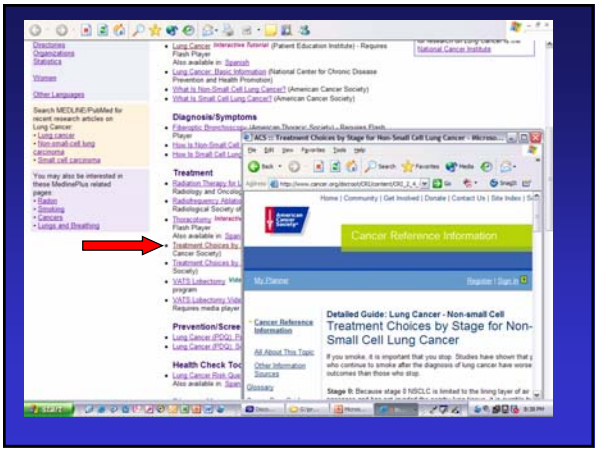


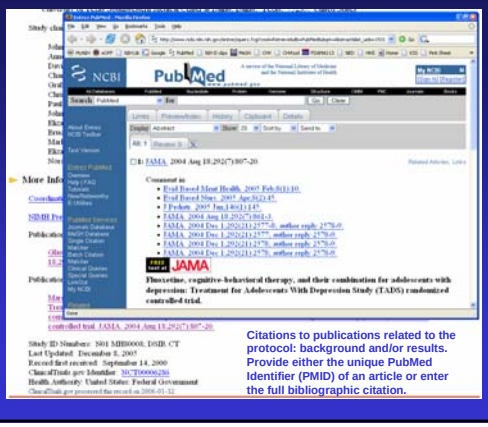






http://www.nlm.nih.gov/medlineplus/tutorials/lungcancer/htm/video.htm





Citations to publications related to the protocol: background and/or results. Provide either the unique PubMed Identifier (PMID) of an article or enter the full bibliographic citation.

Summary

- Many public and private clinical trial web sites provide useful information about clinical trials.
- FDA and NLM will continue to work with:
  - each other
  - pharmaceutical companies and other study sponsors to put required information into the ClinicalTrials.gov
  - health care professionals and patient advocates

How to Contact Us

Office of Special Health Issues
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www.fda.gov/oashi/home.html